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CLAIMS:

1. Use of an expression vector comprising a short hairpin RNA construct under control of a ubiquitous promoter for preparing an agent (shRNA) for constitutive and/or inducible gene knock down in a vertebrate, or in tissue culture or cells of a cell culture derived from a vertebrate.

2. The use of claim 1, wherein the expression vector

(i) is suitable for stable integration into the genome of a vertebrate, or into the genome of the tissue culture or of cells of the cell culture; and/or

(ii) contains homologous sequences suitable for integration at a defined genomic locus through homologous recombination, preferably at a polymerase II dependent locus in the genome of the vertebrate, in the genome of the tissue culture or in the genome of the cells of the cell culture including embryonic cells; and/or

(iii) further contains functional sequences selected from splice acceptor sequences, polyadenylation sites, selectable marker sequences, etc.

3. The use of claim 2, wherein the polymerase II dependent locus is selected from a Rosa26, collagen, RNA polymerase, actin and HPRT locus.

4. The use according to any one of claims 1 to 3, wherein

(i) the ubiquitous promoter is selected from polymerase I, II and III dependent promoters, preferably is a polymerase II or III dependent promoter, most preferably is a CMV promoter, a CAGGS promoter, a snRNA promoter such as U6, a RNase P RNA promoter such as H1, a tRNA promoter, a 7SL RNA promoter, a 5 S rRNA promoter, etc.; and/or

(ii) the ubiquitous promoter is a constitutive promoter, or is an inducible promoter, preferably a promoter containing an operator sequence selected from tet, Gal4, lac, etc.; and/or

(iii) said vertebrate is a non-human vertebrate, preferably is a mouse or fish.

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5. The use according to any one of claims 1 to 4, wherein the expression vector is

- (a) a Pol III dependent promoter, preferably constitutive H1 or U6, driven shRNA construct suitable to be integrated into a ubiquitously active Pol II dependent locus;
- (b) a Pol III dependent promoter, preferably inducible U6 or H1, driven shRNA construct suitable to be integrated into a ubiquitously active Pol II dependent locus; or
- (c) a Pol II dependent promoter, preferably inducible CMV, driven shRNA construct suitable to be integrated into a ubiquitously active Pol II dependent locus.

6. The use according to any one of claims 1 to 5, wherein the shRNA comprises

(I) at least one DNA segment A-B-C wherein

A is a 15 to 35, preferably 19 to 29 bp DNA sequence with at least 95%, preferably 100% complementarity to the gene to be knocked down;

B is a spacer DNA sequence having 5 to 9 bp forming the loop of the expressed RNA hair pin molecule, and

C is a 15 to 35, preferably 19 to 29 bp DNA sequence with at least 85% complementarity to the sequence A; and

(II) a stop and or polyadenylation sequence.

7. A method for constitutive and/or inducible gene knock down in a vertebrate, or in a tissue culture or cells of a cell culture derived from a vertebrate, which comprises stably integrating an expression vector as defined in any one of claims 1 to 6 into the genome of the vertebrate, of the tissue culture or of the cells of the cell culture.

8. The method of claim 7, wherein said vertebrate is a non-human vertebrate, preferably is a mouse or fish.

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9. The method of claim 7 or 8, wherein the expression vector is integrated at a polymerase dependent locus of the living organism, tissue culture or cell culture.

10. The method according to any one of claim 7 to 9, wherein the method for constitutive and/or inducible gene knock down in a vertebrate comprises integrating the expression vector into ES cells of the vertebrate.

11. A vertebrate, or tissue or cell culture derived from a vertebrate having stably integrated, preferably at a polymerase II dependent locus of the vertebrate, tissue culture or cells of the cell culture, an expression vector as defined in any one of claims 1 to 6.

12. The vertebrate tissue or cell culture of claim 11, which is or is derived from a non-human vertebrate, preferably mouse or xfish.

13. An expression vector as defined in any one of claims 1 to 6.

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